REMARKS

Reconsideration of the rejections set forth in the Office action mailed October 11, 2005 is respectfully requested, in view of the following amendments and remarks. Claims 1-36 are pending.

I. Amendments

Independent claims 1, 18, and 29 have been amended, for clarity, to recite that the lecithin starting material contains "phospholipids and triglycerides", in place of "a phospholipid component and a triglyceride component". Support is found, for example, in paragraphs 26 and 48 of the specification as filed.

The independent claims are also amended to recite that the organic solvent medium comprises an aprotic organic solvent and sufficient water to promote hydrolysis. Support is found, for example, in paragraphs 31, 36, 51 and 59 of the specification as filed. These claims are also amended to recite more clearly that the recited substrates are hydrolyzed in the claimed methods. See, for example, paragraph 48 of the specification, lines 1-4.

Claim 1 is amended to recite that an "aqueous medium" refers to a solvent medium containing water and at most 5% of another water-miscible solvent, as recited in paragraph 50 of the specification as filed.

The preamble of claim 29, "A method of producing a hydrolyzed lecithin product, comprising phospholipids, monoglycerides, and diglycerides" has been revised to read "A method of producing a product comprising phospholipids, monoglycerides, and diglycerides by enzymatic hydrolysis".

No new matter is added by any of the amendments.

II. Rejections under 35 U.S.C. §112, Second Paragraph

Claims 1-36 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner continues to state that the term "lecithin" must be interpreted to mean the molecule phosphatidyl choline, as it is often defined in the fields of chemistry and

biochemistry, and thus rejects claims 1-36 as being indefinite.

However, the term "lecithin" is not restricted to this meaning in the fields of foods, edible oils, and food additives, especially in the commercial sense, as discussed further below.

MPEP §2111.01 (II) and (III), which discusses the "plain meaning" of claim terms, cites the following case law (emphasis added):

> If extrinsic reference sources, such as dictionaries, evidence more than one definition for the term, the intrinsic record must be consulted to identify which of the different possible definitions is most consistent with applicant's use of the terms. *Brookhill-Wilk 1*, 334 F. 3d at 1300, 67 USPQ2d at 1137; see also *Renishaw PLC v. Marposs Societa per Azioni*, 158 F.3d 1243, 1250, 48 USPQ2d 1117, 1122 (Fed. Cir. 1998).
>
> Words in patent claims are given their ordinary meaning in the usage of the field of the invention, unless the text of the patent makes clear that a word was used with a special meaning. *Toro Co. v. White Consol. Indus., Inc.*, 199 F.3d 1295, 1299, 53 USPQ2d 1065, 1067 (Fed. Cir. 1999). Also, where an explicit definition is provided by the applicant for a term, that definition will control interpretation of the term as it is used in the claim.

With respect to differing meanings of the term "lecithin", applicants note the following sources (emphasis added):

> "*The term lecithin itself has different meanings* when used in chemistry and biochemistry than when used commercially. Chemically, lecithin is phosphatidylcholine. *Commercially, it refers to a natural mixture of neutral and polar lipids*. Phosphatidylcholine, which is a polar lipid, is present in commercial lecithin in concentrations of 20 to 90%. Most of the commercial lecithin products contain about 20% phosphatidylcholine."
> (http://www.pdrhealth.com/drug_info/nmdrugprofiles/nutsupdrugs/pho_0288.shtml)
>
> "Commercial lecithin, *as used by food manufacturers*, is a *mixture of phospholipids in oil*."

(http://en.wikipedia.org/wiki/Lecithin)

"*Commercial preparations of lecithin* are a complex mixture primarily composed of *phospholipids, triglycerides, fatty acids and carbohydrates*."
(http://www.cfsan.fda.gov/~rdb/opa-g134.html) (FDA; Center for Food Safety & Applied Nutrition)

"*Commercial lecithin* is a naturally occurring *mixture* of the phosphatides of choline, ethanolamine, and inositol, with smaller amounts of *other lipids*."
(21 CFR §184.1400) (Title 21--Food and Drugs; Chapter I--Food and Drug Administration, Department of Health and Human Services; Part 184--Direct Food Substances Affirmed as Generally Recognized as Safe)

Accordingly, the term "lecithin" is used commercially, and in the field of foods and food additives, to refer not to pure phosphatidyl choline, but rather to a mixture which contains phospholipids as well as "other lipids", such as "triglycerides, fatty acids and carbohydrates" (see above).

The applicants in the current application are versed in the food and food additive arts, and therefore they have consistently employed this meaning of the word "lecithin" in the specification, as shown in the following paragraphs (emphasis added):

[0026] Lecithins and modified lecithins are widely used in the food and pharmaceutical industries as digestible solubilizers and emulsifiers. Lecithins are obtained from various animal or vegetable sources, such as soybeans or egg yolk, and **comprise a mixture of phospholipids and triglycerides, as well as lesser amounts of compounds such as glycolipids, carbohydrates, fatty acids, and/or sterols.**

[0048] The process employs **a lecithin starting material having a phospholipid component (preferably at least 50%, and more preferably at least 60%, by weight) and a triglyceride component. Commercially produced lecithins in general fit this description. As used herein, a "lecithin material" or "lecithin starting material"**

refers to a lecithin derived, from a naturally occurring material, such as egg yolk or vegetable oil, e.g. soybean oil, using conventional processing methods, such as described below. The lecithin starting material may include a solvent.

[0050] Phospholipids are separated from the majority of the glyceride oil in the miscella in a process known as "degumming". In conventional water degumming, this is generally done by removing the hexane solvent, hydrating the phospholipids with hot water or steam, which renders them insoluble in hexane, and centrifuging. Removal of some or all of the water gives a **crude lecithin material, typically containing about 60-65% phospholipids (acetone insolubles), with the remainder primarily glycerides, and minor amounts of other components, such as sugars, sterol glucosides, and/or fatty acids.**

In addition, the frequent reference to percent "acetone insolubles", or AI, of lecithins, both by the applicants and in the field, would not make sense if "lecithin" were meant to refer to pure phosphatidyl choline, since the compound itself is completely insoluble in acetone.

In view of the above, the applicants' use of terms such as "lecithin product" or "lecithin material" to refer to materials which contain oils such as triglycerides, in addition to phospholipids, is consistent with accepted commercial terminology and with the definitions and usage provided in the specification. Any attempt to amend or to construe the claims such that "lecithin" refers only to phosphatidyl choline would be inconsistent with the specification.

In view of the foregoing, the applicants submit that the pending claims comply with the requirements of 35 U.S.C. §112, second paragraph.

III. Rejections under 35 U.S.C. §112, First Paragraph

The Examiner states that the monoglycerides and diglycerides formed by the method of claim 29 "are not hydrolyzed lecithin products", and that the specification does not enable the production of monoglycerides and diglycerides by hydrolysis of "a lecithin material" with a lipase that selectively hydrolyzes triglycerides.

To be precise, the original claim language did not in fact recite that monoglycerides and

diglycerides were "hydrolyzed lecithin products". Rather, the preamble recited "*a* hydrolyzed lecithin *product* [in the singular], *comprising* phospholipids, monoglycerides, and diglycerides" (i.e., components of the hydrolyzed product). Nonetheless, the claim preamble has been amended, as described in Section I above, to mitigate this issue.

Moreover, as discussed above, the specification and claims employ the commercial meaning of the term "lecithin", as describing a mixture of components which can include triglycerides as well as phospholipids, not a single type of molecule. Therefore, contacting such a material (which the claim itself defines as "comprising phospholipids and triglycerides") with a triglyceride-selective lipase under conditions of hydrolysis can in fact produce monoglycerides and/or diglycerides.

In view of the foregoing, the applicants submit that the pending claims comply with the requirements of 35 U.S.C. §112, first paragraph.

IV. Rejections under 35 U.S.C. §102(b)

Claim 29 was rejected under 35 U.S.C. §102(b) as being anticipated by Bojsen *et al.*, U.S. Appn. Pubn. No. 2003/0175383. This rejection is respectfully traversed for the following reasons.

A. The Claim

Independent claim 29 is directed to a method of producing a product comprising phospholipids, monoglycerides, and diglycerides by enzymatic hydrolysis, the method comprising:

contacting a lecithin material, comprising phospholipids and triglycerides, in an aqueous medium or an organic solvent medium comprising an aprotic solvent and sufficient water to promote hydrolysis, and in the absence of a phospholipase, with a lipase which selectively hydrolyzes said triglycerides.

B. The Prior Art

The reference describes treating a flour dough with an enzyme that is "capable of hydrolysing a glycolipid and a phospholipid, wherein said enzyme is incapable, or substantially incapable, of hydrolysing a triglyceride and/or a 1-monoglyceride" (Abstract).

The selectivity of the enzyme in this disclosure appears to be the opposite of what is

claimed, since claim 29 recites an enzyme which is not a phospholipase, but rather a lipase which selectively hydrolyzes the triglycerides (as opposed to the phospholipids) in the starting material.

Since the reference does not disclose all of the elements set out in claim 29 and its dependent claims, the claims cannot be anticipated by this reference under 35 U.S.C. §102(b).

V. Rejections under 35 U.S.C. §103(a)

Independent claim 1 and dependent claims 4-6, 14 and 15 were rejected under 35 U.S.C. §103(a) as being unpatentable over Yasukawa *et al.* (U.S. Patent No. 4,976,984) in view of Hattori *et al.* (U.S. Patent No. 5,378,623). The rejections are respectfully traversed in light of the following remarks.

A. The Claims

Independent claim 1 is directed to a method of producing a hydrolyzed lecithin product, comprising hydrolyzed phospholipids, monoglycerides, and diglycerides, the method comprising

(a) contacting a lecithin material, comprising phospholipids and triglycerides, in an aqueous medium, containing water and at most 5% of another water-miscible solvent, or an organic solvent medium, comprising an aprotic solvent and sufficient water to promote hydrolysis, with a first enzyme, said enzyme being a phospholipase or lipase which hydrolyzes said phospholipids; and

(b) subsequently contacting the product of step (a), in an aqueous medium or an organic solvent medium containing sufficient water to promote hydrolysis, with a second enzyme, different from said first enzyme, said second enzyme being a lipase which hydrolyzes said triglycerides.

B. The Cited Art

Hattori *et al.* is cited for its disclosure of various enzymes that can be used to catalyze the hydrolysis of ester bonds in phospholipids. However, it includes no disclosure regarding the use of two different enzymes for the hydrolysis of a composition containing both phospholipids and triglycerides.

Yasukawa *et al.*, the primary reference, describes the advantages of edible oil/fat

compositions having high amounts of diglycerides (i.e. 5 to 100 weight percent of the glyceride component of the composition), as stated in the Abstract. Preferably, the ratio of diglycerides to monoglycerides is 5:1 to 990:1 (column 5, lines 38-39).

This high-diglyceride oil is obtained via one of three disclosed methods (emphasis added): (1) "interesterification of the mixture of glycerol with at least one oil or fat" (column 6, lines 26-28); (2) "esterification of glycerol with unsaturated fatty acids derived from the oils or fats" (column 6, lines 33-35); or (3) use of "fractionated oils from natural edible oils" (column 6, lines 48-50). The reactions of (1) or (2) are preferably carried out using a "1- and 3-site selective lipase" (column 6, line 47) such as Lipozyme 3A (Examples). As described in Examples 1 to 3, at column 7, fatty acids obtained from oils via the action of a 1- and 3- site selective lipase were reacted with glycerol to form the "diglyceride mixtures" (Table 1).

None of the three methods above employs hydrolysis of the oil or fat (triglyceride), as recited in applicants' claims. Esterification of glycerol with fatty acids, or interesterification of oils with glycerol, using a 1- and 3-site selective lipase, as disclosed in Yasukawa, provides a high proportion of diglycerides, as emphasized in the reference.

If, on the other hand, the oils or fats (triglycerides) in Yasukawa were hydrolyzed using a 1- and 3- site selective lipase, a large proportion of monoglycerides would result. This would clearly be undesirable, according to the teachings of the reference, which emphasizes the benefits of high proportions of diglycerides. In fact, the reference states that "Surplus monoglycerides produced by the interesterification or esterification can be removed by molecular distillation or chromatography" (column 6, lines 39-40).

Moreover, this teaching of post-reaction purification of this material, prior to combining it with modified phospholipids to form the final composition, would not suggest that the triglycerides and phospholipids should be combined in the starting material, as in the applicants' claims.

A modification which defeats the purpose of a primary reference, or renders it inoperative, cannot be considered obvious. *In re Gordon*, 221 USPQ 1125 (Fed. Cir. 1984). Therefore, it would not have been obvious to modify the teachings of Yasukawa *et al.* by hydrolyzing a triglyceride using a 1- and 3-site selective lipase, thereby providing monoglycerides, rather than transesterifying glycerol and a triglyceride, thereby providing

diglycerides, as taught by the reference.

In view of the foregoing, the applicant respectfully requests the Examiner to withdraw the rejection under 35 U.S.C. §103(a).

VI. Further Rejections under 35 U.S.C. §103(a)

Dependent claims 2-3, 7-10 and 16-17, independent claim 18, and its dependent claims 19-24 and 27-28 were rejected under 35 U.S.C. §103(a) as being unpatentable over Yasukawa *et al.* (U.S. Patent No. 4,976,984) in view of Hattori *et al.* (U.S. Patent No. 5,378,623), Sas *et al.* (U.S. Patent No. 6,068,997), Haas *et al.* (*J. Am. Oil Chem. Soc.*, 1995), and Chung *et al.* (U.S. Patent No. 6,773,902). The rejections are respectfully traversed in light of the following remarks.

A. The Claims

Independent claim 1, as described above, is directed to a method of producing a hydrolyzed lecithin product, comprising hydrolyzed phospholipids, monoglycerides, and diglycerides, the method comprising

(a) contacting a lecithin material, comprising phospholipids and triglycerides, in an aqueous medium, containing water and at most 5% of another water-miscible solvent, or an organic solvent medium comprising an aprotic solvent and sufficient water to promote hydrolysis, with a first enzyme, said enzyme being a phospholipase or lipase which hydrolyzes said phospholipids; and

(b) subsequently contacting the product of step (a), in an aqueous medium or an organic solvent medium containing sufficient water to promote hydrolysis, with a second enzyme, different from said first enzyme, said second enzyme being a lipase which hydrolyzes said triglycerides.

The rejected dependent claims recite further features such as solvent type, e.g. hexane; enzyme type; and levels of acetone insolubles.

Independent claim 18 is directed to a method of producing a hydrolyzed lecithin product, comprising hydrolyzed phospholipids, monoglycerides, and diglycerides, the method comprising

contacting a lecithin material, comprising phospholipids and triglycerides, in an aprotic

organic solvent containing sufficient water to promote hydrolysis, with first and second enzymes, wherein said first enzyme is a phospholipase or lipase which hydrolyzes said phospholipids, and said second enzyme, different from said first enzyme, is a lipase which hydrolyzes said triglycerides.

The rejected dependent claims recite further features such as solvent type, e.g. hexane; enzyme type; and levels of acetone insolubles.

B. The Cited Art

The Examiner states that Yasukawa *et al.* "are silent as to the nature of the solvent used to perform the hydrolysis of the lecithin and triglycerides". On the contrary, however, as discussed above in Section V.B, Yasukawa *et al.* do not describe "hydrolysis" of triglycerides, but rather interesterification of triglycerides with glycerol, in order to produce a high concentration of diglycerides in the product. Accordingly, the solvent used is glycerol, as described in Examples 1-6 of the reference. Glycerol was also used as solvent and reactant in Examples 7-8, which describe transphosphatidylation between glycerol and soybean lecithin in the presence of a phospholipase. Glycerol is neither "an aqueous medium", an "aprotic organic solvent", nor an organic solvent "containing sufficient water to promote hydrolysis", as recited in the claims.

Hattori *et al.* describes a phospholipase A1 isolated from *Aspergillus*, which selectively hydrolyzes phospholipids to 2-acyl lysophospholipids. Reactions using the enzyme may be carried out in aqueous or organic solvents. Haas *et al.* (1995) describes enzymatic hydrolysis of various triglyceride/phospholipid mixtures, using each of three different lipases and one phospholipase, in water and in water-saturated hexane. Chung *et al.* describe the preparation of high purity lysophosphatidyl ethanolamine by enzymatic hydrolysis of phosphatidyl ethanolamine, or of a different phospholipid in the presence of ethanolamine, using phospholipase A2. The reactions are carried out in "water or organic solvents" (col 4, lines 35-37); the working examples typically employ ethyl acetate/aqueous buffer or diethyl ether/aqueous buffer.

None of the above references include any disclosure regarding the use of two different enzymes, one a lipase and one a phospholipase, for the hydrolysis of a composition containing both phospholipids and triglycerides. Of the above cited references, only Sas *et al.* describes

or suggests hydrolysis of a composition containing both phospholipids and triglycerides, using a combination of enzymes, as claimed.

However, the solvent employed in Sas *et al.* is repeatedly and specifically described as "a water/polyol mixture" or "an aqueous/polyol environment". For the reasons discussed below, it would not have been obvious to modify Sas *et al.* along the lines of the invention by altering this choice of solvent.

C. Analysis

The solvent employed in Sas *et al.* is repeatedly described as "a water/polyol mixture" or "an aqueous/polyol environment"; the working examples employ 6:1 water/glycerol. Sas *et al.* teach that the disclosed method, using a "blend" of enzymes in a water/polyol solvent, gives significantly higher conversion rates of phospholipid to lysophospholipid than prior art processes. For example, Sas *et al.* discloses that over 90% conversion was obtained, vs. about 10-20% for the prior art comparative data (as shown in Tables 1-2 of the patent).

As discussed in the enclosed Declaration under 37 CFR §1.132, the presence of this amount of glycerol would greatly affect the product ratio, by promoting transesterification in place of, or in addition to, hydrolysis.

Moreover, as also discussed in the enclosed Declaration, polyols such as glycerol had long been known, at the time of the invention, to have significant effects on the conformation and activity of enzymes. It is likely that such solvent effects are at least partly responsible for the high conversion of phospholipids to lysophospholipids touted by Sas *et al.* Therefore, one attempting to reproduce this effect would not have any reason to remove the glycerol from the reaction system.

Accordingly, even in view of art describing the use of organic solvents for enzymatic reactions, it would not have been obvious to modify Sas *et al.* along the lines of the invention, by altering their disclosed choice of solvent.

In view of the foregoing, the applicant respectfully requests the Examiner to withdraw the rejections under 35 U.S.C. §103(a).

VII. Further Rejections under 35 U.S.C. §103(a)

Dependent claims 11-13, 25 and 26 were rejected under 35 U.S.C. §103(a) as being

unpatentable over Yasukawa *et al.* (U.S. Patent No. 4,976,984) in view of Hattori *et al.* (U.S. Patent No. 5,378,623), Sas *et al.* (U.S. Patent No. 6,068,997), Haas *et al.* (*J. Am. Oil Chem. Soc.*, 1994), and Chung *et al.* (U.S. Patent No. 6,773,902), and further in view of Jirjis *et al.*, US Pubn. No. 2003/0072856. The rejections are respectfully traversed in light of the following remarks.

A. The Claims

Claims 11 and 25 further limit independent claims 1 and 18, respectively, by reciting that the lecithin material is a retentate from a vegetable oil membrane degumming process.

Claims 12 and 26 further limit independent claims 1 and 18, respectively, by reciting that steps (a) and (b) are carried out in the presence of a membrane effective to separate hydrolyzed phospholipids, monoglycerides, and diglycerides from released fatty acids.

Claim 13 further requires that the solvent comprises an organic solvent (via intervening claim 8).

B. The Cited Art

Each of Sas *et al.*, Hattori *et al.*, Haas *et al.* and Chung *et al.* is discussed above in Sections V and/or VI. The application of this combination of references to independent claims 1 and 18 is described in Section VI.C above. As stated therein, only Sas *et al.* describes hydrolysis of a composition "comprising phospholipids and triglycerides" using a combination of enzymes; the remaining references do not suggest such a process. For the reasons described above, one skilled in the art would not have been motivated to modify the process of Sas *et al.* by employing an aprotic organic solvent in place of the described water/diol mixture.

Jirjis *et al.* describes methods for membrane processing of vegetable oil miscella. An organic solvent such as hexane is generally employed, and "intermediate" solvents are used to condition the membrane. Phospholipids are selectively removed from the miscella to give a primary product (filtrate) which is enriched in oils (i.e. triglycerides) and reduced in phospholipids.

As noted at paragraph 0054 in Jirjis *et al.*, the retentate stream, containing the removed phospholipids, "can be processed into a lecithin product 136 by devolatilizing the solvent". Possible modifications of this lecithin product are described very generally at paragraph 0056.

However, the reference clearly provides no suggestion to employ two different enzymes sequentially, as claimed, to hydrolyze any kind of phospholipid-containing composition.

Accordingly, claim 1 and its dependent claims should be found patentable over this combination of references.

VIII. Further Rejections under 35 U.S.C. §103(a)

Dependent claims 30-36 were rejected under 35 U.S.C. §103(a) as being unpatentable over Bojsen *et al.*, U.S. Appn. Pubn. No. 2003/0175383, in view of Haas *et al.* (*J. Am. Oil Chem. Soc.*, 1994) and/or Jirjis *et al.*, US Pubn. No. 2003/0072856. The rejections are respectfully traversed in light of the following remarks.

A. The Claims

The rejected claims are dependent on claim 29, which recites a method of producing a product comprising phospholipids, monoglycerides, and diglycerides by enzymatic hydrolysis, the method comprising:

contacting a lecithin material, comprising phospholipids and triglycerides, in an aqueous medium or an organic solvent medium comprising an aprotic organic solvent and sufficient water to promote hydrolysis, and in the absence of a phospholipase, with a lipase which selectively hydrolyzes said triglycerides.

The dependent claims further provide, for example, that the solvent medium can be an organic solvent medium (claim 30) and that the lecithin material can be a retentate from a vegetable oil membrane degumming process (claim 31).

B. The Cited Art

Bojsen *et al.*, as described above in Section IV, describes treating a flour dough with an enzyme that is "capable of hydrolysing a glycolipid and a phospholipid, wherein said enzyme is incapable, or substantially incapable, of hydrolysing a triglyceride and/or a 1-monoglyceride" (Abstract). However, as noted above, the selectivity of the enzyme in this disclosure appears to be the opposite of what is claimed, since claim 29 recites an enzyme which is not a phospholipase, but rather a lipase which selectively hydrolyzes the triglyceride component (as opposed to the phospholipid component) of the starting material.

Therefore, even if the process of Bojsen *et al.* were modified to employ an organic

solvent and/or a retentate as described in Jirjis *et al.* (and even if such media were suitable for modifying a flour dough), the process would still not suggest the process of present claims 29-36.

Accordingly, the applicant respectfully requests the Examiner to withdraw the rejections under 35 U.S.C. §103(a).

IX. Conclusion

In view of the foregoing, the applicant submits that the claims now pending are now in condition for allowance. A Notice of Allowance is, therefore, respectfully requested.

If in the opinion of the Examiner a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4403.

Respectfully submitted,

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